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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,538	03/26/2001	Zuomei Li	106101.144	6847

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/817,538	LI ET AL.	
	Examiner	**Art Unit**	
	Terra C. Gibbs	1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *07 September 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: 7.

Claim(s) rejected: *1-3 and 5*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): Applicants reply has overcome the 35 U.S.C. 102 or 35 USC 103 rejection against claim 1 for being anticipated by or obvious over Accession Number AA469268 from NCI-CGAP (National Cancer Institute, Cancer Genome Anatomy Project). Specifically, the oligonucleotide disclosed by NCI-CGAP does not teach or suggest an oligonucleotide having one or more phosphorothioate internucleotide linkages, as now claimed.

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1-3 and 5 remain rejected under 35 U.S.C 103(a) as being unpatentable over Yoshida et al., in view of the collection of Taylor et al., Bennett et al., Baracchini et al., Cowsert, the sequence of HDAC01, and Applicants own admission. In response to this rejection, Applicants argue that there is no motivation or suggestion in the references cited or in the knowledge generally available in the prior art to combine the teachings of the cited references. Applicants argues that the primary reference Yoshida et al. sets forth a technical problem to find a more potent and specific inhibitor of HDAC-1 than n-butyrate and that Yoshida et al. solve this problem by finding another small molecule inhibitor, TSA. Applicants argue that TSA is the more potent and specific inhibitor Yoshida describes a need for, and there is no mention explicitly or implicitly within Yoshida to search outside of the small molecule art for other HDAC-1 inhibitors.

Applicant's arguments have been fully considered, but are not found persuasive. As argued in the previous Office Action mailed July 14, 2004, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the general knowledge of the art indicates that antisense provides a means to specifically inhibit the expression of a target gene for the types of studies proposed by Yoshida et al., this art recognized knowledge is exemplified by the teachings of Taylor et al., and Bennett et al., for example.

As further argued in the previous Office Action mailed July 14, 2004, Yoshida et al. clearly teach that there is a need to find a more potent and specific inhibitor of histone deacetylase for analysis of histone deacetylase activities. Yoshida et al. further discuss how the only other known histone deacetylase inhibitor, n-butyrate, has additional, multiple non-specific effects on cells. Yoshida et al. indicate that TSA appears to be a more specific inhibitor with fewer side effects than n-butyrate, and therefore a useful tool for determining histone deacetylase activities in cells. The skilled artisan would clearly recognize the need to have other specific inhibitors of histone deacetylase as tools in elucidating the function of histone deacetylase, for example, to determine what TSA effects are, in fact, specific for histone deacetylase function, rather than non-specific TSA effects. Activity analysis for histone deacetylase, as taught and motivated by Yoshida et al., clearly would require multiple inhibitors as research tools. Yoshida et al. do not suggest that TSA is the only specific inhibitor needed for this analysis, and further, Yoshida et al. point to the shortcomings of the only other known inhibitor and teach comparative analysis using both inhibitors to elucidate specific versus non-specific effects. The skilled artisan would clearly recognize that other comparative experiments using other specific inhibitors would be useful and that antisense would fulfill that need, based on the teachings of the secondary references and would further recognize the advantages of the improved specificity provided by antisense over the small molecule inhibitors known in the art for HDAC-I. Antisense was a commonly known and art accepted method of inhibition of a target gene in cells in cell culture and thus would have been an obvious choice for making a specific inhibitor of HDAC-I .

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